PEDIATRIC NEWS

San Antonio Military Pediatric Center

Wilford Hall Air Force Medical Center
Brooke Army Medical Center
Darnall Army Community Hospital
www.sampc.amedd.army.mil

October 2003 *Volume 10 Number 5*

Housestaff Puzzler "I Can't Concentrate and My Hair is Falling Out!!" a Case of Mild Thyroid Failure

Damian L. Ternullo Capt MC, PL III
Cydney Fenton LTC MC
Staff Endocrinologist
San Antonio
Military Pediatric Center

HPI: An 11 year old white male with a past medical history significant for mild intermittent asthma, presented to the clinic with a chief complaint of "my hair keeps falling out". He reported that over the preceeding 2 weeks his hair would "just fall out onto my desk". He denied any recent change in soap or shampoo, or applying any products to his hair such as hairspray, moose, or gel. His mother did report that over the past year he had been experiencing increasing stress at school, and that this year he began to fail most of his courses. In the past he was an A/B student. Upon review of his social history, his parents were divorced 5 years

Continued on page 5

In this edition

Neonatal Aeromedical Transport: An Overview

Brian Hall LtCol MC
Chief, Neonatology
San Antonio Military Pediatric Center

Fast forward…

Who: former WHMC pediatric resident, now a new staff pediatrician. **Where:** Elsewhere AB. **What:** Just finished a long day seeing colds, ear infections, sports physicals, and ADHD refills. Time to go home and check out that new sushi bar that opened up just off base.

…Pager…

"You have what?" A 27 year old AD troop who was supposed to ship stateside, but her commander kept her two extra weeks so that she could help with the upcoming JCAHO inspection. She is now 25 weeks gestation and her water broke. OB is having conniptions. The NCOIC is looking for the ventilator but not sure if they can set it up. Would you mind coming to the nursery?!! Oh, and the hospital CO is there already...

The need to transport an unstable/ill newborn may arise in many circumstances, and the above scenario is only one. However, the elements of transport are similar and can be approached systematically. This article attempts to lay out some of these principles and provide

Continued on page 2

Pediatric Pain Syndromes: Common Things Are Common

Daniel F. Battafarano, DO, FACP, FACR
COL, MC, USA
Rheumatology Staff
Brooke Army Medical Center

Introduction: All children experience pain and musculoskeletal pain is quite common. Most musculoskeletal pain is of short duration but many children have more chronic pain without any obvious underlying inflammatory diseases or mechanical skeletal abnormalities to account for their significant level of pain. After undergoing many diagnostic tests and a trial of treatment, children with persistent pain eventually are referred to a rheumatologist for evaluation.

Continued on page 7

a practical guide for how to prepare for and manage these cases in a non-crisis mode.

Introduction: Why Transport?

The simple answer is, of course, to get the patient to the care they need. Ideally, every patient would have whatever medical requirements are necessary wherever they present. However, in a world of limited resources, this is not feasible. The principle of establishing a smaller number of more highly-capable referral centers in a region of less specialized care facilities is called regionalization.

Regionalization offers a number of benefits. Concentrating expensive, complicated technology in referral centers should save money. Also, a planned system of regionalized care allows deployment of assets in a manner not dependent on the local community resources. Similarly, concentrating subspecialists in referral centers helps to maximize their utility and minimize the resources needed to get patients to the subspecialist, since all will be available in a single location, avoiding the need for multiple transfers.

Clearly, a transport system is a critical component of regionalization. The transport system must include sufficient equipment and personnel, must have adequate communications, and must have pre-designated plans for moving patients rapidly. The latter involves three general requirements. The first is ***accurate identification of capabilities***. It is critical that both the referring and referral centers understand what each is capable of doing. It thus becomes incumbent on the new staff pediatrician at a referring center to clarify exactly what capabilities are present at their location, and to find out what the referral center can provide, before the need to transfer arises. Some of the specific issues to determine locally: (a) the form of mechanical ventilation available and who can set it up; (b) verify that the pharmacy has prostin (or better, arrange for enough for one patient to be kept in the nursery; and (c) create a sealed emergency box with supplies for vascular and respiratory access, needle aspiration kit, etc. Issues regarding the referral center include: (a) subspecialties available; (b) ancillary services available (pediatric radiology, CT, MRI); (c) surgical capabilities and options for patients needing cardiothoracic surgery or ECMO; (d) nitric oxide capability; (e) dialysis capability; and (f) transport capabilities and response time.

The next requirement is ***coordination***. This includes communication (you should talk directly with the referral center staff prior to having to arrange a transport), establishment of guidelines of who should be transported, and a detailed step-by-step instruction for arranging transport. This should include names and numbers (and alternatives), clear designation of responsibilities (who will find the driver for the ambulance, etc.), and a mechanism for covering other responsibilities if you are stuck at the bedside of a critical infant. This plan should be made available to the command section so that the appropriate political power is in the loop, in advance.

The final requirement is ***education & training***. An appropriate education and training program includes: at least annual formal training for new personnel using a format such as the STABLE course, designed to teach staff the essentials of stabilization and preparation for transport; and at least quarterly mock transport drills (can be integrated with CPR drills), designed to have the staff practice the principles of stabilization and review the process of arranging transport. Less practice may be needed if the frequency of transport is higher, but a yearly education program is still a must. Ideally, yearly training can be taught by personnel from the referral center.

Patient Options

Option I: Deliver at Location of Presentation. It is ideal for delivery to occur at the referral center. Transport in-utero is much better than infant transport and transferred infants have higher morbidity and mortality. However, local delivery may be the only viable medical option when a patient presents in active labor, or when the infant problems are unknown in advance. Despite the increased risk noted, and much as the local facility may dread the possibility of having to support a critical infant until transfer, the infant still has a better chance with this option than if delivery occurs during transport, regardless of the team involved. It is this author's opinion that a pediatrician should never agree to accompany a maternal transfer "just in case." If there is a significant risk of delivery en-route, maternal transfer should not be attempted. A pediatrician agreeing to do this is setting themselves up for a bad outcome, both medically and potentially legally.

Option II: Local Transfer to Civilian Center. After the infant is born, there are many factors that push to have the infant transferred as soon as possible. A local civilian center may seem to present the best option in this case, and may be the best choice, depending on their capabilities. However, there are sometimes hidden disadvantages. From a medical standpoint, a local civilian transfer may ultimately entail exposing the patient to a second transfer. Also, the local center may exaggerate their outcomes (one of the local Japanese hospitals quoted

a >30% survival expectation for 23 week twins). Medical practice in foreign locales is not necessarily on a par with military referral centers, and there is almost no means available to compare them. There may be significant psychosocial impact on the family due to cultural barriers if the local hospital is in a foreign country. Finally, there may be a substantial monetary cost involved. For example, one long-term hospitalization of a premature infant transferred from Darnall Army Community Hospital to the local civilian hospital resulted in a bill of over $800,000.

Option III: Transfer to Military Referral Center. The remainder of this article will discuss some of the nuts and bolts involved in transferring to a military referral center. Obviously the details will vary depending on the particular centers involved.

Who To Transfer

Acute transfer for elevation of level of care capability is generally justified for: (a) infants born at < 32 weeks EGA or less than 1500 gm birthweight; (b) infants with persistent respiratory distress requiring more than oxyhood support; (c) infants with seizures refractory to usual treatment; (d) infants with congenital malformations or cardiac disorders requiring specialized diagnosis or surgical treatment; and (e) infants with sequelae of hypoxia manifesting for more than 2 hours and with evidence of multisystem involvement.

Transfer on a less acute basis may also be required for: (a) infants requiring prolonged hospitalization in the face of inadequate bed space or staffing; and (b) infants with chronic problems requiring specialized expertise or equipment. As a guideline for estimating length of stay, most premature infants will generally be ready to go home by the time they are 35-36 weeks EGA.

Arranging Transfer

In the continental U.S. (CONUS) all patient transports by military air are coordinated by the Global Patient Movement Requirements Center (GPMRC—not to be confused with the Army's GPRMC, or Great Plains Regional Medical Center). GPMRC is a part of Transportation Command and is located at Scott AFB in Illinois. They don't actually control the planes—they control the patients within CONUS. Movement of overseas patients is controlled by the Theatre Patient Movement Requirements Center (TPMRC), located in Yakota AB, Japan or Ramstein AB, Germany. Overseas patients transferring to CONUS requires coordination between TPMRC and GPMRC. Important to understanding the process is to understand that the system was designed to manage non-emergent movement of adults, and doesn't always do well with emergent movement of infants. The following describes the way it is *supposed* to work:

1. Referring physician submits paperwork (DD form 602 or AF 3899) to their aerovac section, requesting transport
2. Local flight surgeon approves the request for transfer
3. The local A/E section then contacts GPMRC with the request
4. At GPMRC, the Medical Regulator ensures request is complete; the Patient Movement Clinical Coordinator (Nurse) evaluates medical aspects of the request; and the Patient Movement Operations Officer inputs data into a computer system linked to the Tanker Airlift Control Center (TACC)
5. TACC finds a plane that meets the requirements of GPMRC
6. GPMRC alerts the flight crew and finds an A/E crew for the flight and the Duty Controller coordinates mission support (meals, ambulance) through local A/E sections
7. The transporting center A/E contacts the transport team and arranges ground transport
8. The A/E crew provides in-flight medical care

Obviously, there are many "contacts" and steps built into this process, any one of which can cause delay. In practice, some short-cuts are typically done: (1) the referral center physician usually contacts GPMRC directly to alert them of the need for transport and to get things rolling more quickly, (2) the PMCC at GPMRC handles all aspects of GPMRC function for urgent requests, (3) in some places, such as WHMC, civilian contracts allow bypassing military transport if it is going to take too long, (4) A/E sections are notified in parallel, but physicians on each end contact GPMRC directly, (5) the on-board A/E crew is minimized or waived entirely as they have no expertise in transporting infants. Unfortunately, these "shortcuts" are not usually formalized and tend to have to be rediscovered when staff changes occur.

Preparation For Transport

Before the transport team arrives (in fact, before transfer is requested) the referring physician should discuss with the family the infant's medical condition, the reasons for transfer, the destination, and the transfer process. A step-by-step concrete description of what will happen is helpful. Parents are under a great deal of stress during these times and may have difficulty seeing the overall picture. Do not make promises about outcome, but do reassure the parents regarding the capabilities of the transport team and referral center. If possible,

obtain extra copies of any parent handouts that the referral center has and provide these to the parents in advance. The parents should also sign consent for transfer.

The referring physician must remain in communication with the referral center and provide updates on the patient's condition. This should happen every 1-2 hours or if there are any significant status changes.

The referring center retains responsibility for the medical care of the patient until they leave the facility. In practice, the transport team will begin to manage the patient on arrival, but the referring physician should maintain oversight of what is going on. Medical care in the case of a complicated case may be guided by consultation with the referral center, but at a minimum the following should be done:

1) Establishment of 2 secure sites of vascular access, preferably including 1 central line
2) Establishment of arterial access for patients on respiratory support
3) Secure ETT documented in proper position
4) Decompression of any air leak with chest tube placement
5) Placement of OG or NG tube to maintain gastric decompression in-flight
6) Blood gas results timed close to transport team arrival
7) CXR/KUB for patient on respiratory support or with central lines
8) Recent set of electrolytes, CBC
9) Copy of chart, including H&P, progress notes, nursing notes, flow sheets, orders, radiographs, medication administration record and lab results. Include pertinent maternal data such as prenatal labs.

The use of surfactant is slightly controversial. Some worry that a patient treated with surfactant may be more difficult to manage during transport as compliance changes at the same time that the patient is undergoing altitude changes. However, the compliance changes with surfactant occur relatively quickly after treatment and in my opinion if the treatment is indicated it should not be delayed for transport.

The use of prostin is another issue that arises in the case of a suspected cardiac anomaly. There are only a few cardiac conditions in which the use of prostin on a short-term basis will potentially cause the patient to worsen, so in general for any case of a suspected ductal-dependent lesion we recommend that prostin be started. It is important to be aware of the side effects of fever and apnea that can result and it is important to get the medication on early enough to be able to evaluate for these in advance of the transport. Some advocate "prophylactic" intubation when prostin is used.

Having medications and drips on syringe pumps rather than in roller pumps can facilitate the transfer as the transport team will only use syringe pumps.

If You Do The Transport

In almost all cases, urgent neonatal transport will be done by a transport team from the referral center. At Wilford Hall you may participate on the transport team missions, but in order to fly you must have completed appropriate egress training. In order to lead an air mission, you must also have taken the neonatal transport course, which is offered yearly in the fall. The elements of this course are too extensive to cover in this article. The following are simply a few of the general principles to keep in mind should you end up as a staff member being the "only game in town."

Flight Issues

Barometric pressure changes. Fixed wing aircraft are routinely pressurized to 8,000 feet equivalent pressure. At this pressurization gas expands approximately 30% compared to its volume at sea level. The pneumatic ventilators used in transport deliver an increased volume of gas when taken up in altitude, so it may be necessary to turn down the peak inspiratory pressure slightly during assent and back up during descent. Lower barometric pressure can also cause problems due to trapped gas. It is essential to have an open OG tube for any infant on positive pressure ventilation. {Question: how would you handle an infant with a TE fistula and esophageal atresia +/- anal atresia?) One alternative is to pressurize the plane to a lower equivalent altitude, although this requires the plane to use more fuel and fly slower.

Humidity. Air at altitude is colder and holds less moisture, so there is a tendency for patients and staff to dehydrate during long air transports. This can especially be a problem for patients on mechanical ventilation. Because of the electromagnetic interference with navigation equipment produced by electric humidification systems used in the hospital, these are not used in-flight. Patients on a ventilator can develop thickened secretions and plugs, potentially leading to obstruction—patients have died due to this. It is critical to maintain patient hydration and to conserve and/or add moisture to the ventilator system (for example: 1-2cc NS down the ETT every hour).

Temperature. Maintaining adequate temperature support for neonates on a transport can be quite

challenging. Chemical warming pads should always be a part of the transport supplies for a neonatal transport. Even during the summer it is cold at altitude!

Vibration and turbulence. Equipment used on military medical flights must first pass testing at Brooks AFB to ensure that it can function under the stresses of air transport. Nevertheless vibration can cause degradation in monitor functioning, can cause equipment to fall apart or fall off, and can cause ETTs to come disconnected. It is important to continually re-assess equipment function during an air transport. It is also important to make sure that everything is fastened down. Sudden turbulence can create lethal projectiles out of otherwise life-saving medical equipment.

Noise. Aircraft are very noisy environments. Because it may not be possible to hear alarms the medical staff must constantly keep their eyes on the patient and the support equipment. This is extremely boring and fatiguing, but is the only way to ensure that problems are caught early. Because it is difficult to hear each other the medical staff need to write down key communications to be sure there is no misunderstanding. Verbal orders have little place on the ground and NO place in the air. Because it is almost impossible to assess the patient by listening, it is critical that monitors work, that tubes and lines are secure before starting, and that staff maintain heightened alertness during the transport.

Conclusion. Obviously, this article only hits the tip of the iceberg. Neonatal air transport is a huge subject that literally encompasses all aspects of neonatal care with the added complication of doing it while moving, at altitude, with limited resources. For more information, see:

1. Wilford Hall Neonatal Transport Manual
2. Evaluation, Stabilization, and Transport of the Critically Ill Child, Aoki BY & McCloskey K, ed., Mosby Year Book, 1992.
3. AFI 11-2AE Aeromedical Evacuation, Aircrew Training
4. AFI 41-301, 302 Aeromedical Operations.

Continued from page 1

ago, but he gets along with both of them and by his own report has adjusted fairly well. Of note, he recently had entered middle school. Mother denied any behavioral problems but did state that he had a hard time actually sitting down and doing his homework. He denied having difficulty understanding his schoolwork, but was unable to determine why he was doing so poorly in school. He did state that he has trouble concentrating.

Past Medial History: Mild intermittent asthma "well controlled."

ROS: Upon further review of systems he denied constipation, diarrhea, heat or cold intolerance and there was no recent weight loss or gain. He had been having some increased congestion, itchy eyes and scratchy throat for 2-3 months and had been awakening in the morning with congestion.

Physical exam: No chart was available but his height and weight were in the 15th percentile.

BP: 105/61, HR: 87, O2 Sat: 99% RA, temp: 98.3 (orally)

Gen: alert, thin nontoxic well groomed boy who appeared his stated age.

HEENT: NC/AT conj clr, Tms clr, inf turb red and inflamed, no transverse nasal crease, no allergic shiners, post pharynx clear no cobblestoning

Hair: soft, did not fall out with running hands through it, upon plucking hair the root was examined using the otoscope magnifying head but no clubbing was visualized

Neck: supple no mass or goiter

Remainder of the exam was unremarkable

Oupatient Course/ Decision Making

Pt was diagnosed with allergic rhinitis and prescribed Allegra D and Flonase. He was told to follow up in 10 days with a letter from his teachers at school, concerning his schooling.

Follow Up Appointment

His allergy symptoms had improved. However, he still complained of decreased ability to concentrate at school and easy distractibility. His grades had worsened to the point where he was failing many of his subjects. Physical exam was unremarkable.

Plan

Neuropsychometric testing was requested to be done at school secondary to the possibility that he may have a learning disorder. His thyroid function was assessed due to concerns for hypothyroidism causing his symptom of inability to concentrate, and he was placed with a continuity physician to help form rapport with this child.

His thyroid function tests (TFTs) returned with Thyroid stimulating hormone (TSH) at 9.3 (0.4-4.2) and Free thyroxin 1.3 (0.7-1.8). This was confirmed on repeat screening with a TSH of 9.1, Free T4

of 1.0, and thyroid peroxidase (TPO) antibodies of 26 (<2). Both his antithyroglobulin and anti-microsomal antibody titer were unremarkable.

Discussion

The differential diagnosis (prior to obtaining the lab studies) of this child's problem is varied and broad. See Table 1 for differential diagnosis.

Both adjustment disorder/ depression may require multiple visits to fully determine if indeed either of these are the etiologies of his chief complaint.

Table 1

Differential diagnosis

Adjustment disorder
Depression
Alopecia
Telogen effluvium
Hypothyroidism
Learning disorder
ADHD

Telogen effluvium is characterized by loss of hair that many times is initially noted by parents of children when brushing their hair. It is an acute onset form of alopecia. It is purely a reactive process characterized by an arrest of the hair growth cycle in the telogen phase (or resting phase). In most people only 5-15% of their hair follicles are in this phase of the growth cycle at one time, but with telogen effluvium a large number of hairs enter this phase at once. There are many causes that trigger this and these include any stressors on the body such as acute/chronic illnesses, changes in diet, medications (beta blockers, anticoagulants, vitamin A, PTU, and immunizations). This can last up to 3-6 months and is usually self limiting. It can be diagnosed by close examination of the scalp, looking for higher than expected number of short new hairs growing. One can also estimate the duration of hair shedding by measuring the length of the shortest hairs, as typical hair growth is 1cm per month. There should also be no bald patches on the scalp. Certainly this child could have had this but it would not explain his "poor concentration" at school.

Acquired hypothyroidism can have multiple causes. (Table 2)

This discussion will concentrate on primary hypothyroidism as this is more common than central (secondary) hypothyroidism. It is important to note that the most common cause of hypothyroidism worldwide is iodine deficiency, and second most common is chronic autoimmune thyroiditis.

The incidence of Hashimoto's Thyroiditis (HT) peaks in mid puberty. Clinical manifestations of hypothyroidism in general include inability to concentrate, hair loss, constipation, fatigue. Some common physical exam findings include goiter (although not in our child), dry skin, coarse hair. The typical thyroid gland in HT is diffusely enlarged and has a rubbery consistency.

Table 2

Central (secondary) hypothyroidism
- Pituitary hormone deficiencies
- Idiopathoic
- Pituitary tumor
- CNS radiation

Primary Hypothyroidism
- Endemic goiter
- Chronic autoimmune thyroiditis
  - Hashimoto's thyroiditis
  - Atrophic thyroiditis
- Drug induced hypothyroidism
- Mild thyroid failure

This disorder can be diagnosed by the presence of high serum titers of antithyroid antibody, namely antithyroid peroxidase (Anti-TPO) or antimicrosomal antibodies. Anti TPO antibodies may play a role in blocking the organification of iodine which is important in the formation of thyroxine.

Our patient has mild thyroid failure or subclinical hypothyroidism. Some physicians refer to this form of hypothyroidism as "compensated hypothyroidism". Many physicians feel that although the body requires more TSH to stimulate the thyroid gland, patients still have "normal" thyroid hormone levels and are therefore euthyroid. In reality this is not the case at all. The half-life of T4 is 7days, T3 is 1 day and TSH is 1 hour. With these values known one would expect TSH to return to normal with circulating normal leves of T3/T4. However with our child with mild thyroid failure this is not the case. Therefore thyroid hormone is insufficient thus increasing the level of TSH. This disease state represents an early stage of hypothyroidism, and progression to frank hypothyroidism occurs in up to 20 percent of individuals. There have been multiple studies evaluating these patients demonstrating cognitive impairment and memory loss.

Treatment is still somewhat controversial, there have been three randomized controlled trials evaluating the role of L-thyroxine in these patients. 2/3 studies demonstrated improvement in symptoms and a return of the TSH level to normal values. Some endocrinologists/pediatricians still elect to follow these patients and observe the TSH levels. One recent study demonstrated that in adults greater than 35 y/o treating mild thyroid failure is as cost effective as many other screening procedures. Many physicians also

decide to treat on the presence of anti thyroid antibodies. Members of the American Thyroid Association (ATA) when polled stated that if anti-thyroid antibodies were positive 95% of those physicians polled would treat.

There are many important learning points in this case…

1. The importance of follow up in our population can never be underestimated
2. ADHD clinically did not "fit" in this case as their was no history of ever having had any attention/learning problems prior to this presentation, and the diagnosis of ADHD in this age group without a history of these problem prior to the age of 6 is very difficult
3. In adolescence a good HEADSS exam should always be done as some of his symptoms (hair falling out, inability to concentrate) could potentially be attributed to depression or an adjustment disorder considering he had just recently started in a new school and the timing of his problems coincided with this.
4. In the presence of anti-thyroid antibodies in patients with mild thyroid failure it is many physicians practice to begin synthroid as treatment.

Bibliography and Suggested Reading:

1. www.Endotext.com
2. www.emedicine.com
3. McDermott, Michael T., Ridgway, E.Chester., Subclinical Hypothyroidism Is Mild Thyroid Failure and Should be Treated., Journal of Clinical Endocrinology and Metabolism 2001;86:10:4585-4590
4. Koch, CA., Sarlis, NJ., The Spectrum of Thyroid Diseases in Childhood and its Evolution During Transition to Adulthood: Natural History, Diagnosis, Differential Diagnosis and Management., Journal of Endocrinological Investigation., 2001; 24:9:659-675
5. Fisher, D.A., Hypothyroidism., Pediatrics in Review 1994; 15:227

Continued from page 1

Incidence and Prevalence

Surveys of children reflect that musculoskeletal pain is a frequent cause of visits to the school nurse and the pediatrician. Back pain has been reported as high as 20 %, limb pain in 16 % and fibromyalgia (FM) in 6 %. The incidence and prevalence of other idiopathic musculoskeletal pain syndromes has increased in recent years and is diagnosed in 6-8 % of new patients by pediatric rheumatologists.

Differential Diagnosis

The differential diagnosis for musculoskeletal pain syndromes can be very extensive (Table 1). Systemic diseases, neoplasia or inflammatory musculoskeletal syndromes occur in ill-appearing children with abnormal laboratory screening tests including inflammatory indicators like the erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). The combination of plain radiographs, bone scans, computerized tomography (CT) and/or magnetic resonance (MR.) imaging have greatly enhanced the ability to diagnose bony and soft tissue disease processes. Subspecialty consultations are often necessary for the more complicated genetic, metabolic or systemic causes of musculoskeletal pain syndromes. Hypermobility, growing pains, and FM are most common compared to the other rare diagnoses. The most common pain syndromes only require a careful history and physical examination for a diagnosis although laboratory and radiographic screening may be essential to exclude less likely etiologies for the pain.

Table 1

Differential Diagnosis in children with musculoskeletal syndromes

- Hypermobility
- Neoplasia
- Growing pains
- Pernio (chilblains)
- Fibromyalgia
- Spinal cord tumors
- Primary Raynaud's syndrome
- Chronic recurrent multifocal osteomyelitis
- Spondyloarthropathy
- Fabry disease
- Myofascial pain
- Peripheral neuropathy
- Chronic compartment sydromes
- Erythromelalgia
- Transient migratory osteoporosis
- Thyroid disease
- Progressive diaphyseal dysplasia
- Vitamin D deficiency

Generalized hypermobility occurs in 10-20 % of Caucasians and even higher in Chinese and East Africans. Girls are twice as likely to be hypermobile as boys. Hypermobility can be associated with Marfan's or Ehlers-Danlos syndromes, both of which are uncommon connective tissue disorders. However, the majority of children with hypermobility syndrome present between ages 3 and 10 years. The pain most often involves the leg muscles and behind the knees. Wrist and hand pain may also occur. The symptoms may be

short-lived or may occur after prolonged playing of soccer or swinging on the monkey bars often associated with hyperextension of the knees and elbows/hands respectively. The pain may be most severe toward the end of the day or can awake the child from sleep with crying. The children do not have morning stiffness or limping. On routine examination, there is no inflammation or muscle atrophy of the involved areas. These children typically meet the Carter and Wilkinson criteria for hypermobility. The criteria include: 1) touching either thumb to the volar forearm, 2) hyperextension of the metacarpophalangeal joints of one hand so that the fingers are parallel with the forearm, 3) greater than 10 degrees hyperextension of either elbow, 4) greater than 10 degrees hyperextension of either knee, and 5) able to touch the palms to the floor with the knees straight. Children with three out of five criteria are considered to have the generalized hypermobility syndrome. Education and reassurance are the primary treatments for hypermobility. Acetaminophen or nonsteroidal anti-inflammatory agents (NSAIDs) may be helpful as needed for symptoms. This syndrome resolves with increasing age and stronger supportive muscles.

Recurrent patellar dislocation is sometimes considered localized hypermobility. This is manifested by a sudden giving way of the knee with pain and an inability to straighten the leg with the knee held in 25 degrees flexion. The patella dislocates laterally because of congenital abnormalities of the patella (unifaceted or bipartite patella), of the femoral condyles (shallow intercondylar groove) or of the patellar ligament (lateral attachment). Repeated episodes of dislocation lead to premature degeneration of the articular cartilage of the patellofemoral joint. Also, growth related factors influence the development of patellofemoral mechanics. The history should carefully screen for periarticular soft tissue or joint injuries that may have resulted in cartilage damage. Examination can easily reproduce the pain on manual manipulation of the patella and may reveal patellar tracking problems or weakened quadriceps muscles. The primary treatment approach is strengthening of the vastus medialis muscle to centralize the patella, improve the patellofemoral mechanics and alleviate the pain syndrome. Ice, rest, elevation, acetaminophen or NSAIDs may benefit the child in the acute or chronic setting while physical therapy is ongoing. Occasionally, surgical realignment of the extensor system may be necessary.

Patellofemoral pain syndrome is an overuse injury that can become chronic and this is distinctly different from recurrent patellar dislocation. It is characterized by pain and tenderness in the medial patellar facet and crepitation on movement of the joint. A small effusion may be present. If the syndrome is associated with fissuring and fibrillation of the posterior surface of the patella then this is referred to as chondromalacia patella. This retropatellar knee pain occurs most commonly in teenage girls with activities that stress the quadriceps such as deep knee bends, climbing or descending stairs or running. Pain recurs after prolonged sitting with the knee flexed and is relieved by extension of the leg. Activities that provoke the pain should be stopped and strengthening of the quadriceps, especially the vastus medialis muscle, should be pursued. Analgesics and anti-inflammatory medications may be indicated for brief periods. A knee strap or elastic support may provide additional relief during the rehabilitation period.

Growing pains occur in 10-20 % school aged-children and most frequent in elementary or pre-school ages. The pains occur in early evening or may awaken the children from sleep. The pain is crampy and usually involves the thigh, shin or calf and is relieved with massage. The children do not have any morning stiffness, limping or residual pain. The examination and laboratory or radiographic evaluations are normal. The diagnosis of hypermobility should be excluded. The etiology of growing pains is unknown. However, this pain syndrome is benign and although it is referred to as growing pains, the actual rate of growth is not associated with these pain symptoms. Children are successfully treated with reassurance, decreasing secondary gain, and massage. Acetaminophen or NSAIDs are occasionally used for pain relief or prevention of pain.

Amplified musculoskeletal pain syndromes are divided into localized idiopathic pain or diffuse idiopathic pain. Localized idiopathic pain is defined as persistent pain localized to one limb for 1 month or for 1 week after medical treatment once previous trauma or potential diseases have been excluded. Examples of localized idiopathic pain include myofascial pain or reflex sympathetic dystrophy with autonomic dysfunction. Diffuse idiopathic pain is generalized musculoskeletal aching in three or more sites for greater that 3 months only after the exclusion of potential disease processes that could explain the symptoms. The most common examples of diffuse idiopathic pain are FM and psychosomatic pain.

Fibromyalgia is a well described syndrome among adults manifested by chronic widespread pain involving all four quadrants of the body (and the axial skeleton) with the presence of discrete tender points associated with fatigue and a nonrestoring sleep pattern. In 1993, Buskila et al assessed the prevalence of FM in children to be approximately 6% among 338 consecutive

healthy school children. Subsequent pediatric rheumatology studies reflect similar findings for FM. Since that time, pediatricians consider the diagnosis of FM in children with diffuse idiopathic pain although they have limited clinical experience with this pain syndrome.

The typical patient with FM is a preadolescent to adolescent girl (mean age 12 years) from an upper-middle class family. Frequently, an obvious interdependency between the mother and child is observed during an office visit through body language and with the mother answering all of the questions even when addressed directly to the patient. Children with FM are more likely to be depressed and fatigued, have non-restorative sleep and have multiple somatic complaints. Common somatic complaints include headaches, abdominal pain, dysmenorrhea and hyperventilation. They do not have autonomic complaints like extremity sweating or skin color changes nor do they manifest allodynia (unable to bear light touch) on examination. Symptoms of pain may temporarily improve with massage, heating pads, or exercise but not significantly with acetaminophen or NSAIDs.

Sometimes children have a la belle indifference about both the pain and the dysfunction it causes when they describe the severe pain in almost a cheerful manner. These children are often mature and excel in school. Parents may describe these children as having perfectionist, empathetic characteristics with an eagerness to please others even at their own personal expense. Children with FM may have experienced a major life event such as divorce, moving, change of school, death of a family member or friend or have a history of physical or sexual abuse.

The physical examination is normal except for the presence of 11 of 18 classic tender points (in soft tissue) for FM (Figure 1). Occasionally, children will have less than 11 tender points. The tender point locations are bilateral and symmetrical. The anatomic points are located at the occiput (suboccipital muscle insertions), trapezius (midpoint of the upper border), supraspinatus (above the medial border of the scapular spine), gluteal (upper outer quadrant of the buttocks), low cervical (anterior aspect of the intertransverse space of C5-7), 2nd rib (costochondral junction), lateral epicondyle (2 cm distal to epicondyle) greater trochanter (posterior to trochanteric prominence) and the knee (medial fat pad proximal to the joint line). Tender points are tested by direct digital pressure of 3-4 kg (enough to blanch the nail) in a perpendicular direction with the skin. Patients with FM have normal control points with palpation over the forehead, dorsum of mid-radius, shin, clavicle or thumbnail. When a patient is tender even over the control points, the musculoskeletal examination is unreliable and psyhchosomatic pain syndrome should be considered.

Blood tests are normal with FM including ESR and CRP unless there is a concurrent illness. Serologies for thyroid disease and other connective tissue diseases should be screened to exclude any systemic diseases that could be associated with FM. Radiographs, bone scans and other imaging studies are not indicated or diagnostic for FM.

The cornerstone of treatment for FM is patient and family education. Although FM can cause significant dysfunction, it is not life threatening. It should be explained that the etiology for FM is poorly understood but is classically associated with diffuse tender points, a non-restorative sleep pattern, fatigue and often depression in the absence of any disease process. Cognitive-behavioral therapy and counseling for coping with chronic pain and assessing for any psychological triggers for FM should be pursued in young patients with FM.

Physical therapy modalities such as muscle stretching and strengthening, massage and moist heat are helpful. Aerobic exercise with or without formal team sports provides relief of tender points and often improves the quality of sleep. Analgesic treatment with acetaminophen or NSAIDs has had variable benefit but are conventionally prescribed for pain relief. In general, corticosteroids and narcotic analgesics should be avoided in the treatment of FM.

If education, physical therapy, exercise, analgesics and counseling are unsuccessful then medications that increase serotonin levels should be considered. These medications tend to improve the quality of sleep, decrease the intensity of the tender points, and improve cognitive function with daily activities. They may also be helpful if depression is a significant part of the clinical syndrome. Cyclobenzaprine, tricyclic antidepressants and the selective serotonin-reuptake inhibitors (SSRIs) have all been used successfully in pediatric patients with FM.

Unfortunately, there are few outcome studies looking at the natural history of FM and/or treatment in children. These studies include small numbers of children making it difficult to extrapolate significant conclusions. In general the outcome of FM in children is considered more favorable than adults. Approximately, 30-50% of the children report some pain after 5 years but 90% are not disabled. It is speculated that children with significant underlying psychological triggers may be more inclined to relapse or have chronic FM.

Conclusion

Pediatric pain syndromes are frequently encountered in the pediatric clinic. Hypermobility, recurrent patellar dislocation, patellofemoral syndrome, growing

pains and FM can be diagnosed with a careful history and physical examination. Subspecialty consultations may be necessary for complicated pain syndromes but common things are still common in everyday practice.

References

Bowyer S, Roettcher P. Pediatric rheumatology clinic populations in the United States: Results of a 3-year survey. J Rheumatol 1996; 23:1968-1974.

Buskila D, Neumann L, Hershman E, et al. Fibromyalgia syndrome in children-an outcome study. J Rheumatol 1995:22:525-528.

Carpenter MT, Hugler R, Enzenauer RJ, et al. Physical and sexual abuse in female patients with fibromyalgia. J Clin Rheumatol 1998;4:301-306.

Okifuji A, Turk DC, Sinclair JD, et al: A standardized manual tender point survey. Development and determination of a threshold point for the identification of positive tender points in fibromyalgia syndrome. J Rheumatol 1997; 24:377-383.

Sherry DD, Malleson PN. The idiopathic musculoskeletal pain syndromes in childhood. Rheum Dis Clin N Am 2002;28:669-685.

Sherry DD, Malleson PN. Idiopathic musculoskeletal pain syndromes. In Cassidy JT, Petty RE (eds): Textbook of Pediatric Rheumatology. Philadelphia, W.B. Saunders, 2001, pp 381-394.

Thabit G, Micheli LJ. Patellofemoral pain in the pediatric patient. Orthop Clin North Am

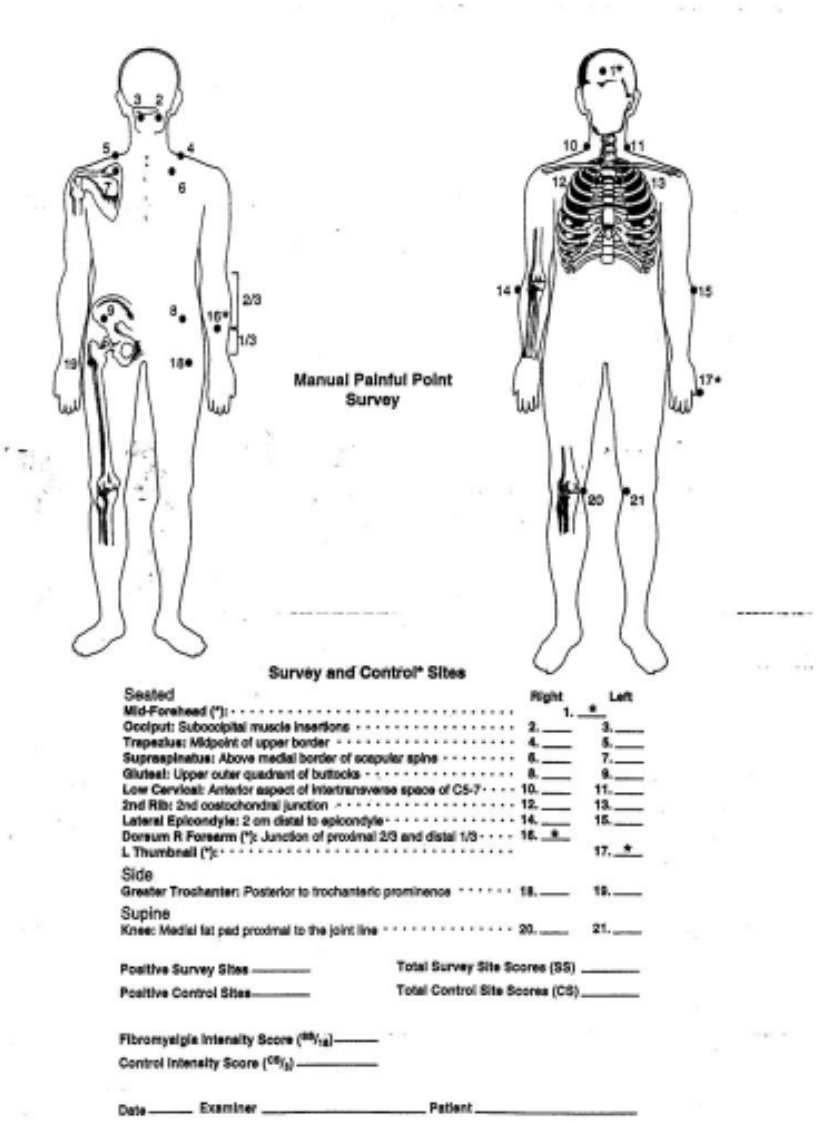

Figure 17–1. Diagram of painful points in fibromyalgia as defined by the American College of Rheumatology:[11] (From Okifuji A, Turk DC, Sinclair JD, et al: A standardized manual tender point survey: I. Development and determination of a threshold point for the identification of positive tender points in fibromyalgia syndrome. J Rheumatol 24: 377–383, 1997.)

Pediatric Puzzler
Primary Amenorrhea

Tracy Alderson Capt MC PLIII
San Antonio
Military Medical Center

A 16 7/12 year old Caucasian female presented to Pediatric Endocrinology for further work up of delayed puberty. She initially presented to her PCM complaining that she had not yet started having periods. She stated that she had noticed breast development about one year prior to presentation, and reported needing to shave her legs once every 2 weeks, but had not yet experience menarche. She denies body odor, acne, recent weight gain or loss, sexual activity, or any problems with masculine type hair growth. Past medical history revealed that she had essentially been a healthy young lady, with an unremarkable birth, and early development. Her review of systems was negative for a history of head trauma, seizures, visual disturbances or headache. The patient was a good student, having just completed the junior year of high school. Her family history was negative for any sexual ambiguity, or delayed puberty. Her mother experienced menarche at 12 years of age.

Pertinent physical exam findings revealed a moderately obese, articulate young woman. Vitals were within normal limits. Her weight was 80kg (almost 96%) and her height was 168cm (75%). Height and weight were plotted on a growth chart from birth, and revealed consistent heights from 50-90% and weight that had been consistently 75-95% with no sudden jumps or drop-offs. Her visual fields were intact. Her neck was supple without thyromegaly. She had Tanner 2 breast development with rare striae. No axillary hair was noted. Her Genitourinary exam revealed a normal appearing Tanner 2 female, well estrogenized. A pelvic exam had been performed by her PCM and was reportedly hindered by not being able to pass a speculum, and an inability to palpate the cervix. However, her hymen was patent. Her skin exam revealed no hyperpigmentation.

Initial laboratory and radiological data obtained by her PCM was:

WBC 6.7 x 10^3/mm^3
HGB 13.7g%
HCT 40%
PLT 346 x 10^3/mm^3
HCG (urine) negative
U/A color: yellow
appearance: clear
gluc: neg
bili: neg
Ket: neg
SG: 1.010
Blood: neg
pH: 7.0
Prot: neg
Urobil: 0.2
nitrite: neg
Leuko est: neg
SERUM (mg/dL): Gluc: 90
BUN: 12 Cr: 0.7 Na+: 144
K+: 4.2 Cl-: 103 CO2: 24
TSH 2.028 uIU/mL (0.49-4.67)
FSH 104.36 mIU/mL (3.7-12.9)
LH 31.85 mIU/mL (0.9-14)
Prolactin 11.35 ng/mL (1.39-24.2)

MRI Pelvis:
"No ovaries evident via this modality which corresponds to the patient's absent secondary signs…. There may be a small vestigial rest of partially formed uterine tissue near the apex of the bladder however."

Pelvic Ultrasound:
"Prepubertal uterus with streak ovaries in normal position."

DISCUSSION:
An organized approach to the evaluation of delayed menses begins with a basic understanding of the normal progression of female puberty. Puberty is the process that achieves three goals: 1. secondary sexual development 2. attainment of reproductive capacity 3. secondary wave of skeletal growth and attainment of adult stature. The first change in the initiation of puberty is an increase in growth velocity. Thelarche (breast development) generally occurs between 9-11 years of age in the U.S. followed by adrenarche (characterized by the development of pubic hair). Recent data, however, have suggested that up to 15% of Caucasian adolescents experience adrenarche first, and that perhaps even a majority of African American females experience adrenarche before thelarche. Classic teaching remains that breast development is the first sign of puberty in girls. Menarche occurs during the deceleration phase of growth, which is generally about 12.8 years of age in the U.S.[1]

Puberty is described as being clinically delayed if sexual maturation is not apparent by 13 years of age in females, or if menarche has not occurred by 16 years of age or within 5 years of pubertal onset. It is important to note that this definition is based on statistical norms, so that approximately 2.5% of healthy adolescents will meet the criteria of delayed puberty. [2]

When evaluating delayed puberty in a female, it is helpful to classify the patient according to estrogen exposure.

1. Hypoestrogenism/ hypogonadism. This is characterized by a complete pubertal delay (a lack of breast development and amenorrhea). This is caused by either (a) ovarian failure (hypergonadatropic) or (b) hypothalamic-pituitary immaturity of suppression (hypogonadotropic)
2. Normal estrogen/ eugonadism. This is characterized

by an isolated delay in menarche and is caused by either (a) congenital absence of the uterus and/or the vagina (b) chronic anovulation (e.g. Polycystic Ovary Disease) (c) an intersex disorder (e.g. androgen insensitivity).[3]

Our patient had a complete pubertal delay with elevated FSH and LH, leading to the diagnosis of ovarian failure.

High levels of gonadotropins characterize primary ovarian failure. Its causes are either congenital (gonadal dysgenesis, steroidogenic blocks, resistant ovaries), acquired (oophrectomy, oophoritis, radiotherapy or chemotherapy), or bioinactive gonadotropin. The most common cause of primary ovarian failure is Turner Syndrome, making it important to check chromosomes in all girls with primary amenorrhea. Gonadal dysgenesis may also occur with Turner Mosaicism, or with Trisomy 21, 13 or 18.

Autoimmune oophoritis is another important cause of primary ovarian failure. It is the etiology in 1/3 of all cases and may be associated with autoimmune thyroiditis, diabetes, or polyendocrine failure. It is also associated with autoimmune adrenal failure, which usually occurs first, and may be associated with nonendocrine autoimmune disorders like Lupus and Rheumatoid Arthritis.

Savage Syndrome is ovarian resistance to gonadotropin action. It is caused by LH and FSH receptor defects and is autosomal recessive. Albright's osteodystrophy (pseudohypoparathyroidsm) is often associated.[4]

Several other genetic disorders are in the differential for primary ovarian failure. These include galactosemia, blepharophimosis, and myotonia dystophica.

During her endocrinological evaluation several other labs were obtained.

Estradiol: 17 pG/mL (16-132)
Estrone: 25 pG/mL
Testosterone: <20 pG/mL
Sex Hormone Binding Globulin: 14 nmol/L (17-120)
Ovarian Antibodies: negative
Karyotype: 46 XX; FISH for SRY: negative

Due to the discrepancy in the MRI and ultrasound findings, a laparascopic evaluation was performed by a pediatric urologist which revealed a rudimentary uterus and normal appearing ovaries in the appropriate position.

A diagnosis of idiopathic primary ovarian failure with normal 46XX, SRY negative karyotype was made, and the patient was started on premarin for 6 months, at which time she should be changed to a standard low dose oral contraceptive pill.

References

1. Reindollar R, Lalwani S. Abnormalities of Female Pubertal Development. Endotext.com- Female Reproductive Endocrinology.2002: http://www.endotext.org/female/female2/female2.htm

2. Rosen D, Foster C. Delayed Puberty. Pediatrics in Review. 2000;

PRIMARY OVARIAN FAILURE DIFFERENTIAL

CONGENITAL	ACQUIRED	GENETIC
Gonadal dysgenesis	Oophrectomy	Fragile X associated
Steroidogenic blocks	Oophoritis	Trisomies
Resistant ovaries	Radio/Chemotherapy	Galactosemia
		Blepharophimosis
		Myotonia dystrophica

Editor's note: Erratum - Apologies to Dr. Martha Schatz who was noted to be a Pediatric Dentist in the last issue. Dr. Schatz is a Pediatric Ophthalmologist.

John Baker, M.D.
Editor, *Pediatric News*
Department of Pediatrics
San Antonio Uniformed Services Pediatrics
jabaker@texas.net